

Claims 1-13 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Claims 1-13 have also been rejected under 35 U.S.C. §102(b) as being anticipated by “Pharmacology and Biological Efficacy of a Recombinant, Humanized, Single-Chain Antibody C5 Complement Inhibitor in Patients Undergoing Coronary Artery Bypass Graft Surgery With Cardiopulmonary Bypass” written by Fitch et al, published by Circulation in 1999 (hereinafter referred to simply as “Fitch”). These rejections are respectfully traversed.

Before specifically addressing the rejections, however, a brief summary of the presently claimed subject matter may be helpful.

Claims 1-13 are directed to a method of prophylaxis against large myocardial infarctions in patients undergoing a procedure that involves cardiopulmonary bypass (CPB). Prophylaxis is achieved by administering an effective myocardial infarction-reducing amount of an anti-inflammatory compound to patients undergoing a procedure that involves CPB.

The term prophylaxis is used in its ordinary sense to mean a preventive treatment. The treatment *prevents* large myocardial infarction in CPB patients. A large myocardial infarction is defined in applicants’ specification as those which exhibit peak blood levels of CK-MB greater than about 50ng/ml. (See, Specification at page 3, lines 23-25.)

The present methods do not require determining or predicting post-operative blood levels of CK-MB prior to administering the compound. Rather, in accordance with the present disclosure, the prophylaxis treatment is given to patients undergoing a procedure that involves CPB. Applicants have surprisingly found that such prophylactic

treatment significantly decreases the likelihood of a CPB patient experiencing a large myocardial infarction.

Turning now to the rejection under 35 U.S.C. §112, first paragraph, the Office Action alleges that: “[t]he specification is not enabling for the claimed invention because there is no disclosure of the identification of the subject group of patients prior to administration of an anti-inflammatory agent and the separation of those subjects from patients below the respective claimed thresholds prior to anti-inflammatory compound administration or operative procedures.” (Office Action, Page 3, lines 8-11) The Office Action goes on to suggest the patient pool does not satisfy the metes and bounds of the claim (Office Action, Page 3, line 20) because the post-operative CK-MB blood level can not be determined pre-operative.

It is respectfully submitted that the present claims are being misconstrued. As previously stated, the method of prophylaxis is intended to be used in connection with patients undergoing a procedure that involves CPB. The pool of patients undergoing such CPB procedures is readily identifiable. Further, the reference in the claims to threshold CK-MB levels (e.g., to “peak blood levels of CK-MB greater than about 50ng/ml” in claim 1) refers to *the type of large myocardial infarctions prevented* by the presently claimed prophylactic treatment. The threshold CK-MB levels do not determine the metes and bounds of the patient pool. Because the identification of the subject group of patients receiving the claimed prophylactic treatment is clearly described in applicants’ specification as patients undergoing a procedure that involves CPB, withdrawal of the rejection of claims 1-13 under 35 U.S.C. §112, first paragraph is deemed appropriate and is respectfully requested.

With respect to the rejection of claims 1-13 under 35 U.S.C. §102(b) as being anticipated by Fitch, nowhere does Fitch teach or suggest any methods for *prophylaxis against myocardial infarction* in patients undergoing a procedure that involves CPB.

Rather, Fitch merely makes the general statement that the “reported incidence of MI after CABG surgery ranges from 1% to 10%” (see page 11 of Fitch) and then discloses some general data and conclusions about “myocardial injury”. These conclusions include the statements “C5 inhibition significantly attenuates postoperative myocardial injury” (see Conclusions section on page 2) and “...the potent inhibitory and anti-inflammatory effects of h5G1.1-scFv were associated with significant reductions in postoperative myocardial injury.” (see top of page 11). These general statements by Fitch regarding reductions in myocardial injury do not anticipate the present claims to methods of prophylaxis against myocardial infarctions and do not form a basis for concluding that the present claims to methods of prophylaxis against myocardial infarctions would be obvious.

Fitch also fails to report post-operative, peak CK-MB levels in patients undergoing a procedure that involves CPB. Rather, Fitch merely reports total (i.e., cumulative) CK-MB levels. Specifically, in the “Analysis of Myocardial Injury” section on page 8, Fitch states:

“To assess myocardial injury, the *total release of CK-MB was measured* during the 24 hours after drug administration. Total CK-MB was significantly less ($P<0.05$) in patients treated with 2.0 mg/kg h5G1.1-scFv than in those given placebo...” (Emphasis added.)

Furthermore, in the legend to Figure 4 on page 8 Fitch states:

“Myocardial injury was determined in CPB patients by measurement of the ***cumulative release of CK-MB*** over 24 hours.” (Emphasis added.)

Because Fitch fails to report post-operative, individual CK-MB levels in patients undergoing a procedure that involves CPB, Fitch cannot possibly anticipate the presently claimed methods of prophylaxis against myocardial infarctions which exhibit blood levels of CK-MB greater than about 50ng/ml. Furthermore, Fitch’s disclosure of total (i.e., cumulative) CK-MB levels does not render obvious the presently claimed methods of prophylaxis against myocardial infarctions which exhibit blood levels of CK-MB greater than about 50ng/ml. Fitch simply has no disclosure one way or the other with respect to any increase or decrease in myocardial infarctions of the recited magnitude.

In addition, Fitch states on page 11 that based on his cumulative findings, “there does not appear to be a threshold effect”. However, the present inventors have shown using measurements of peak CK-MB blood levels (as compared to Fitch’s cumulative data), that an anti-inflammatory compound provides significant prophylaxis only against ***large*** myocardial infarction (i.e., myocardial infarction where the peak CK-MB level is greater than about 50 ng/ml). More specifically, as seen in Figure 2 of applicants’ specification, the placebo and anti-inflammatory compound curves diverge significantly only for peak CK-MB levels in excess of 50 ng/ml. This unexpected result is nowhere taught or suggested by Fitch, who only reports cumulative CK-MB levels and makes general conclusions regarding “myocardial injury.”

Lastly, the relationship between International Units (IU) and Nano-Grams/mL (ng/ml) is irrelevant. As stated above, Fitch reports cumulative data for the amount of CM-KB found in the CPB patient’s blood during the 24 hours following the initial dose

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given. In the present disclosure, the blood levels of CM-KB were monitored for up to 4 days (Page 9, line 15) post-operatively to discover the peak CK-MB blood level. Since Fitch's cumulative results provide no insight into peak blood level measurements, the difference between IU and ng/ml is irrelevant.

Accordingly, because Fitch: 1) fails to teach or suggest any methods for *prophylaxis* against myocardial infarction in patients undergoing a procedure that involves CPB; 2) fails to report post-operative, *individual CK-MB level readings* in patients undergoing a procedure that involves CPB; and 3) fails to recognize that an anti-inflammatory compound provides significant prophylaxis *only against large myocardial infarction* (i.e., myocardial infarction where the peak CK-MB level is greater than about 50 ng/ml), withdrawal of the rejection of claims 1-13 under 35 U.S.C. §102(b) as anticipated by Fitch is deemed appropriate and is respectfully requested.

In view of the foregoing, this application is believed to be in condition for immediate allowance. Such early and favorable action is earnestly solicited.

Respectfully submitted,



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